

Role of Serotonin in Memory by Tryptophan Loading Method among First Year Medical Students

D.D. Musmade¹, Vivek Nalgirkar², Disha Chaudhary³, Krishnakhi Deba³, Sarthak Pawar³, Pritesh Jadhav³

¹Ph.D. Scholar, ²Prof. and Head, ³Medical Student, Dept. of Physiology, Dr. D.Y. Patil Medical College, Nerul, Navi Mumbai

Abstract

Serotonin is a widely studied compound with known effects on mood, memory, emotions and other neuropsychiatric parameters. The present study was conducted to assess the effects of serotonin increase on memory among first year medical students. The study was done using tryptophan loading method, which was given to the subjects over a period of ten days. Pre and Post administration questionnaires were used to assess their memory, while serotonin levels were also estimated before and after the study. The results revealed that administration of serotonin has an impact on memory among the selected study subjects.

Keywords: Memory, Medical Students, Serotonin.

Introduction

Serotonin (5-hydroxytryptamine, 5-HT) has been linked to emotional and motivational aspects of human behavior, including anxiety, depression, impulsivity, etc. Several clinically effective drugs exert effects via 5-HT systems.⁽¹⁾ Growing evidence suggests that these effects play an important role in learning and memory. Whether the role of serotonin is related to memory and/or behavioral or emotional aspects remains an important question.⁽²⁾ A key question that remains is whether 5-HT markers (e. g., receptors) directly or indirectly participate and/or contribute to the physiological and pharmacological basis of memory and its pathogenesis.

Cognitive dysfunctions (eg. dysfunctions in the processing of neutral as opposed to emotional information) associated with depressive disorders have been subject of many studies.^(3,4) Other studies have compared the effects of tryptophan loading with the effects of tryptophan depletion on cognitive functioning, mood and neuroendocrine measures (prolactin and cortisol) in healthy participants.⁽⁵⁾ The studies concluded that in healthy subjects enhancement of the serotonin

precursor may lead to impaired affective working memory but also to enhanced attention and recognition of fear and happiness. Sub-chronic effects include an increased recognition of happiness and a decreased recognition of disgust as well as a decreased processing of negative stimuli. These cognitive changes seem to be unrelated to changes in mood. Tryptophan loading seems to have a broader range of effects on cognitive performance compared to the effects of receptor-agonist and antagonist administration.⁽⁶⁾

The present study was conducted to ascertain the effect on memory on healthy adult subjects who a tryptophan loading diet, while measuring their serotonin levels before administration and after completion of the study.

Methodology: The present study was a prospective study conducted at Dr. D. Y. Patil Medical College, Hospital and Research center, Nerul, Navi Mumbai. In this study participants were first year medical students aged between 18 to 25 years.

Institutional ethical clearance was obtained prior to starting the study.

Total number of participants was 20, comprising of 10 male and 10 female participants without any pre morbidities and not on any medications. Daily 30 gms of protein powder was given to participants in morning at the same time for 10 days. Serotonin level of blood was

Corresponding Author:

Dr. Vivek Nalgirkar

Prof. and Head, Dept. of Physiology, Dr. D.Y. Patil Medical College, Nerul, Navi Mumbai

e-mail: physiology@viveknalgirkar.com

measured before and after completion of 10 days period by using a Serum Enzyme Immunoassay (EIA) method. The effect of serotonin on their memory was assessed before and after study period, using standard validated questionnaires. The data was analyzed before and after administration by using SPSS statistical analysis software, in consultation with institutional statistician.

Observations: The mean age of the study group was 19.95 years all the subjects successfully completed the entire trial within the stipulated study period. The mean serotonin levels were 161.87 ng/ml with a standard deviation of 48.78 before the trial, and mean serotonin levels post administration was 166.65 ng/ml with a standard deviation of 48.54. Males had average level of 145.16 ng/ml pre-administration of protein, while after 10 days, the mean level was 151.05ng/ml, denoting an increase of 5.89ng/ml. Females had a mean level of 178.59 ng/ml pre-administration of protein, while after 10 days, the mean level was 182.26 ng/ml denoting an increase of 3.67 ng/ml.

Analysis of Pre and Post administration of protein powder levels of serotonin revealed a p value < 0.001, denoting that a statistically significant difference in mean serotonin levels among the study group. No statistically significant difference was observed in the values among males and females in terms of mean serotonin levels.

Table 1: Results of Memory Testing Questionnaire

Parameter	Pre Administration	Post Administration	P Value
Short term Memory	Intact (14) Impaired (6)	Intact (16) Impaired (4)	<0.001
Long term Memory	Intact (12) Impaired (8)	Intact (16) Impaired (4)	<0.001
Immediate Recall	Able (11) Unable (9)	Able (13) Unable (7)	<0.001
Forgetfulness	Commonly (9) Sometimes (8) Rarely (3)	Commonly (6) Sometimes (11) Rarely (3)	0.0318 (NS)

(Numbers in Brackets denote subjects), (P value calculated at 95% Confidence Interval, NS-Not Significant)

The analysis of the results revealed that in terms of short term memory testing, 30% (n=6) had impaired memory pre administration, and post administration, the number reduced to 20% (n=4) among the selected study sample. A statistically significant relationship was seen in the number of candidates with improved scores in

short term memory testing. Similar trend was observed in long term memory testing and immediate recall questions among the selected study subjects (Table 1). The data revealed a statistically significant relationship between long term memory and immediate recall in post administration group who had been given protein powder. In contrast, on self assessment of forgetfulness experienced by the candidates, no significant difference was observed in the study population.

Discussion

The present study revealed a relationship between administration of protein and levels of serotonin in otherwise healthy subjects. There was no significant difference in serotonin levels based on age or gender among the selected study population. This is in concurrence with studies by Musmade et al and leibowitz, who did not find significant changes in serotonin levels based on gender. However the subjects displayed a statistically significant difference in terms of changes on short term and long term memory in the selected study population. This change is in concurrence with studies by Murphy and Markus^(7, 8), who reported that a protein rich diet increases cognitive function in individuals, while depletion of the same causes a reduction in effective memory. However, our study is not in concurrence with the findings of Harmer⁽⁹⁾, who found that short term memory does not show significant changes upon ceasing use of serotonin reuptake inhibitors while long term memory shows significant improvement on same parameters. We observed statistically significant changes in both long and short term memory among our study population.

A variety of studies have mentioned that the direct participation of 5-HT is seen in enhanced brain serotonin activity by means of its precursor (i.e., tryptophan) and led to improved memory in animals (Haider et al.) and normal elderly people and AD, Parkinson's disease and schizophrenia patients (Levkovits et al; Porter et al), whereas, in human and animals, decreased brain 5-HT levels through acute 5-HT depletion impaired memory (Evers et al; Schmitt et al.)⁽¹⁰⁻¹⁴⁾

It has been reported that Nutrition exerts a positive effects on brain function. Animal studies indicate increased endogenous plasticity as the underlying mechanism in terms of the activation of neuronal precursor cells in different brain areas, which leads to improved brain function at multiple sites of the central

serotonergic system, increasing the volume of grey matter in learning-and memory-associated brain regions, and improving cognitive function. This phenomenon opens up noninvasive causal therapeutic options in neurodegenerative disorders and during aging-associated cognitive decline by inducing changes in lifestyle. ⁽¹⁵⁾

Conclusion

Our study concluded that minor improvements in memory can be elicited by use of nutritional supplementation in healthy subjects. This could possibly pave the way for further research in novel therapeutic interventions in the memory enhancement of various types of patients and in other diseases under conditions of memory formation, amnesia or forgetting and should be explored in the near future. Together with the improved diagnostics of the disease, new therapeutic interventions will cause further specialization, with increased treatment and caring costs amplified by the ever-growing number of patients with memory disorders. Our study is limited by the low number of study participants.

Conflict of Interest: Nil

Source of Funding: Self Funded

References

1. Aloyo VJ, Berg KA, Spampinato U, Clarke WP, Harvey JA. Current status of inverse agonism at serotonin_{2A} (5-HT_{2A}) and 5-HT_{2C} receptors. *Pharmacology & therapeutics*. 2009 Feb 1; 121 (2):160-73.
2. Barnes NM, Sharp T. A review of central 5-HT receptors and their function. *Neuropharmacology*. 1999 Aug 1; 38 (8):1083-152.
3. Deuschle M, Kniest A, Niemann H, Erb-Bies N, Colla M, Hamann B, Heuser I. Impaired declarative memory in depressed patients is slow to recover: clinical experience. *Pharmacopsychiatry*. 2004 Jul; 37 (04):147-51.
4. Wagner S, Müller C, Helmreich I, Huss M, Tadić A. A meta-analysis of cognitive functions in children and adolescents with major depressive disorder. *European child & adolescent psychiatry*. 2015 Jan 1; 24 (1):5-19.
5. Musmade DD, Nalgirkar V, Satav J, Chaudhari P, Pradyumna T. Role of Serotonin on Appetite in first year medical students. *Sch J App Med Sci* 2019, 7 (2):775-777.
6. Leibowitz SF, Alexander JT. Hypothalamic serotonin in control of eating behavior, meal size, and body weight. *Biological psychiatry*. 1998 Nov 1; 44 (9):851-64.
7. Murphy F, Smith K, Cowen P, Robbins T, Sahakian B. The effects of tryptophan depletion on cognitive and affective processing in healthy volunteers. *Psychopharmacology*. 2002 Aug 1; 163 (1):42-53.
8. Markus CR, Olivier B, de Haan EH. Whey protein rich in α -lactalbumin increases the ratio of plasma tryptophan to the sum of the other large neutral amino acids and improves cognitive performance in stress-vulnerable subjects. *The American journal of clinical nutrition*. 2002 Jun 1; 75 (6):1051-6.
9. Harmer CJ, Shelley NC, Cowen PJ, Goodwin GM. Increased positive versus negative affective perception and memory in healthy volunteers following selective serotonin and norepinephrine reuptake inhibition. *American Journal of Psychiatry*. 2004 Jul 1; 161 (7):1256-63.
10. Haider S, Khaliq S, Ahmed SP, Haleem DJ. Long-term tryptophan administration enhances cognitive performance and increases 5HT metabolism in the hippocampus of female rats. *Amino Acids*. 2006 Nov 1; 31 (4):421-5.
11. Levkovitz Y, Ophir-Shaham O, Bloch Y, Treves I, Fennig S, Grauer E. Effect of L-tryptophan on memory in patients with schizophrenia. *The Journal of nervous and mental disease*. 2003 Sep 1; 191 (9):568-73.
12. Porter RJ, Lunn BS, O'BRIEN JT. Effects of acute tryptophan depletion on cognitive function in Alzheimer's disease and in the healthy elderly. *Psychological medicine*. 2003 Jan; 33 (1):41-9.
13. Schmitt JA, Wingen M, Ramaekers JG, Evers EA, Riedel WJ. Serotonin and human cognitive performance. *Current pharmaceutical design*. 2006 Jul 1; 12 (20):2473-86
14. Evers EA, Tillie DE, Van Der Veen FM, Lieben CK, Jolles J, Deutz NE, Schmitt JA. Effects of a novel method of acute tryptophan depletion on plasma tryptophan and cognitive performance in healthy volunteers. *Psychopharmacology*. 2004 Dec 1; 177 (1-2):217-23.
15. Strüder HK, Weicker H. Physiology and pathophysiology of the serotonergic system and its implications on mental and physical performance. Part I. *International journal of sports medicine*. 2001 Oct; 22 (07):467-81.